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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,078	04/28/2005	Shunsuke Ishii	P27813	2400
7055 7590 10/18/2007 GREENBLUM & BERNSTEIN, P.L.C. 1950 ROLAND CLARKE PLACE RESTON, VA 20191			EXAMINER EPPS FORD, JANET L	
			ART UNIT 1633	PAPER NUMBER
			NOTIFICATION DATE 10/18/2007	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/533,078

Applicant(s)

ISHII ET AL.

Examiner

Janet L. Epps-Ford

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 13-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-12, and 25, and species SEQ ID NO: 2 in the reply filed on 8-01-07 is acknowledged. The traversal is on the ground(s) that the Office did not set forth a comparison between the claims and the art, instead the action relied upon 37 CFR § 1.475 as the basis for restriction. According to Applicants stating that the possibility that unity of invention *might* not be present is not sufficient to establish lack of unity. This is not found persuasive because as stated in the prior Office Action, the instant claims are drawn to multiple products, therefore as per 37 CFR § 1.475(d) if multiple products are claimed, the first invention of the category first mentioned in the claims of the application, and the first recited invention of each of the other categories related thereto will be considered as the main invention of the claims, see PCT Article 17(3)(a) and §1.476(c). Moreover, as indicated by the international search report, Xia et al. discloses constructs that produce a 21 base pair siRNA hairpin directed against eGFP. This prior art disclosure establishes that the invention set forth in at least instant claim 1 does not make a contribution over the prior art and therefore does not share any special technical features with the invention set forth in group II as set forth in the prior Office Action, and therefore lacks unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 13-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or

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linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8-01-07.

3. Claims 1-12 and 25 are therefore currently under examination.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-4 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Xia et al. (published online September 16, 2002).

6. Xia et al. discloses a construct that expresses an siRNA of 21 base pairs that forms a hairpin structure, wherein the hairpin comprises a sequence that is complementary to enhanced green fluorescent protein. The hairpin was placed under the control of the CMV promoter and comprised a poly(A) cassette. This disclosure meets the limitations of instant claims 1-4. Xia et al. also teach transfection of these constructs into mammalian cells, particularly HEK-293 cells(see page 1006). This disclosure meets the limitations of instant claim 25.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-4 and 7-8 rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. (as applied to claims 1-4 and 25) in view of Perkins et al. (US 2003/0119104 A1) and Yonaha et al.

9. Xia et al. discloses constructs encoding a hairpin structure under the control of RNA polymerase II. However, Xia et al. does not teach (1) constructs comprising a pause site.

10. Perkins et al. teach recombinant vectors comprising with the following elements: immediate/early human CMV enhancer/promoter with intron A, multiple cloning sites, a pause site from the human alpha 2 globin gene, see paragraph [0316], and a polyA SV40 terminator sequence (see paragraph [0317]). Perkins et al. also teach that the constructs of their invention can be used to express siRNA, and that the siRNA encoding sequences can be placed under the control or regulation of a regulatable or inducible promoter that would allow one to temporally and/or spatially control the knockdown effect of the corresponding gene, see paragraph [0077].

11. Additionally, Yonaha et al. discloses the use of MAZ sequences as pause sites that function to both pause Pol II transcription and activate polyadenylation.

12. It would have been obvious to the ordinary skilled artisan at the time of the instant invention to modify the constructs of Xia et al. with the teachings of Perkins et al. in the design of the instant invention. One of ordinary skill in the art would have been motivated to modify the teachings of Xia et al. with the construct elements of Perkins et al. since the constructs of Perkins et al. are disclosed for the same purpose as the

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constructs of Xia et al., namely for the efficient expression of nucleic acid, including siRNA, in mammalian cells.

13. Absent evidence of the unexpected results, the ordinary skilled artisan would expected to have had a high degree of success in designing constructs for the expression of siRNA following the teachings according to Xia et al. in view of Perkins et al. since both references provide sufficient guidance in designing constructs for the expression of siRNA. Moreover, since Yonaha et al. presents the MAZ domain, it cannot be considered to be especially difficult to substitute the MAZ domain into the constructs of Xia et al. and Perkins et al. for the activation of polyadenylation.

14. Claims 1-6 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. (as applied to claims 1-4, and 25) in view of Huang et al.

15. The discussion of Xia et al. as set forth above is incorporated here, however, Xia et al. does not disclose a construct for the expression of a hairpin and a ribozyme.

16. Huang et al. discloses a construct for the production of a transcription product comprising a stem-loop (or hairpin) structure and a ribozyme.

17. It would have been obvious to the ordinary skilled artisan to modify the constructs of Xia et al. with the ribozyme constructs of Huang et al. to comprise the expression of both a hairpin and ribozyme. The ribozyme constructs of Huang et al. were designed to control the polyadenylation of the transcript product, and thereby regulate the nuclear export of the transcript. The ordinary skilled artisan seeking to design alternative constructs for expressing hairpin comprising transcripts would have been motivated to design the constructs according to the present invention since the addition of the

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autocatalytically cleavable ribozyme would enhance the functionality of the transcript produced by the prior art constructs.

18. Claims 1-4, and 10-12, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. in view of Nomura et al. and GenBank accession No. AF435852.

19. The discussion of Xia et al. as set forth above is incorporated here, however Xia et al. does not teach constructs targeting the *ski* gene.

Nomura et al. describes the *ski* gene as a proto-oncogene, moreover this reference teaches that overexpression of this gene results in the oncogenic transformation of embryonic fibroblast. Moreover, Nomura et al. teach that overexpression of the *ski* gene in transgenic mice results in hypertrophic growth. The sequence of the mouse *ski* gene is disclosed in the prior art as GenBank Accession No. AF43582.

It would have been obvious to the ordinary skilled artisan to modify the teachings of Xia et al. with the teachings of Nomura et al. and GenBank Accession No. AF43582 in the design of the instant invention. Absent evidence to the contrary the ordinary skilled artisan would have been motivated and would have had a reasonable expectation for success in designing dsRNA constructs according to Xia et al. targeting the *ski* gene, since the prior art describes the dsRNA constructs as useful for targeting any given gene, and the prior art discloses the *ski* gene as a disease-related gene. Moreover, since a sequence encoding a *ski* gene was disclosed in the GenBank

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database, it would have been a simple task for the ordinary skilled artisan to design a dsRNA construct targeting this sequence.

Claim Rejections - 35 USC § 112

20. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

21. Claims 5-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

22. Claim 5 recites the ds-RNA expression vector according to claim 1, which further comprises a sequence that autocatalytically cleaves *RNA located upstream* of the nucleotide sequences (a) to (c). Claim 1 does not provide proper antecedent basis for the limitation "*RNA located upstream*" of the nucleotide sequences (a) to (c). It is unclear which RNA sequences Applicants are referring to.

23. Claim 6 recites the ds-RNA expression vector of claim 5, wherein the sequence that autocatalytically cleaves RNA is a ribozyme site. The metes and bounds of the phrase *ribozyme site* are vague and indefinite, since it is unclear if the term site is intended to encompass a nucleotide sequence that encodes a ribozyme, or a sequence that is recognized by a ribozyme for cleavage.

24. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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25. Claims 1-12 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Written description).

26. The instant claims are drawn to expression vectors generically comprising (a) a nucleotide sequence encoding a part of a target gene, or a nucleotide encoding DNA that hybridizes to a sequence complementary to a target gene, and a sequence complementary to (a) and an inverted repeat thereof, and a loop region, wherein the target gene is a disease associated gene, wherein the target gene is the Ski gene, and further wherein the vector comprises a pause sequence that is *a sequence of the MAZ domain*.

First it is noted that applicants have not defined constructs a hairpin structure targeting *a part of* any and all disease associated genes, including for example, all polymorphic and allelic variants of Ski gene, mutated forms of these genes, and variants of these genes isolated from any source natural or synthetic.

See the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement. These guidelines state: "[T]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed

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invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention.

The specification as filed discloses SEQ ID NO: 1, which is a 540 base pair region of a Ski gene. However, this disclosure is insufficient to describe constructs targeting all variants of disease-associated genes, or all variants of the Ski gene. Moreover, the disclosure does not provide an adequate description of a MAZ domain, or further wherein which part of said MAZ domain would function as a pause site. As per MPEP § 2163, "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

Applicant's specification does not provide an adequate description of the full scope of constructs encompassed by the instant claims.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
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JLE